

**REMARKS**

This paper is being filed in response to the Office Action dated May 21, 2002.

Applicants request a one-month extension of time and enclose the fee required under 37 C.F.R. §1.17(a)(1). Applicants submit herewith a Supplemental Information Disclosure Statement and copies of the cited documents. Applicants also enclose herewith a Second Substitute Sequence Listing in paper and computer readable form. Applicants respectfully request reconsideration of the above-identified application in light of the amendments and remarks presented in the instant Amendment.

Claims 1-36 are pending. Claims 1, 2, 4-7, 11, 24-28, 31, and 34-36 have been cancelled. Claims 3, 8-10, 12-23, 29-30, and 32-33 have been amended. New claims 37-44 have been added. Rewritten claims and specification paragraphs appear in the preceding "IN THE CLAIMS" and "IN THE SPECIFICATION" sections. Attached hereto is a marked-up version of the changes made by the instant amendment captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE" and is included pursuant to 37 C.F.R. §1.121(c)(ii). Should any discrepancies be discovered, the version presented in the preceding "IN THE CLAIMS" and "IN THE SPECIFICATION" sections shall take precedence.

Amended claims 3 and 8 and new claim 37 are supported by the application as filed at, *inter alia*, page 8, lines 13-16, page 14, lines 29-33, Figure 5, and original claims 1, 3, and 8. Claims 3, 8 and 37 recite amino acid sequence identity of at least 50%. Applicants respectfully invite the Examiner's attention to the specification at page 8, lines 13-16, wherein Applicants define polypeptides as homologous "if the amino acid sequence of the first polypeptide exhibits a similarity of at least 50% on the polypeptide level to the amino acid sequence of the second polypeptide." Applicants assert that "similarity" in the context of this

definition means identity. Support for this assertion may be found at page 14, lines 29-33 and Figure 5. Figure 5 shows a sequence alignment of *Arabidopsis thaliana* MSH3 (AtMSH3)(SEQ ID NO:19) and *Saccharomyces cerevisiae* MSH3 (ScMSH3)(SEQ ID NO:102), wherein the only indication of similarity depicted is that of identity. See Figure 5, inverted blocks. This is intended, in part, to clarify that, while the AtMSH3 and ScMSH3 **nucleic acid sequences** are homologous according to the conventional definition of "homologous" in the art as stated at page 14, lines 29-33, the **amino acid sequences** are not homologous according to the definition of "homologous" provided in the specification at page 8, lines 13-16. Therefore, claims 3, 8, and 37 are fully supported by the application as filed and do not constitute new matter.

Amended claims 9-10, 12-23, 29-30, and 32-33 are fully supported by the application as filed, *inter alia*, at original claims 9-10, 12-23, 29-30, and 32-33, and, therefore, do not constitute new matter.

New claims 38-44 are fully supported by the application at, *inter alia*, at Figure 5, SEQ ID NO:19, and original claims 3, 13, and 17-21 and, therefore, do not constitute new matter.

**I. Substitute Sequence Listing Complies with Requirements**

The Examiner has stated that the Sequence Listing presently of record fails to comply with the requirements of 37 C.F.R. §§ 1.821 through 1.825 for allegedly failing to include sequences recited at page 12, lines 36-37 of the specification.

Applicants traverse this objection and assert that the Sequence Listing of record complies with 37 C.F.R. §§ 1.821 through 1.825 in that the pentapeptide sequences disclosed at page 12, lines 36-37 are contained within either SEQ ID NO:19 (AtMSH3) or SEQ ID NO:31 (AtMSH6). Therefore, Applicants respectfully request withdrawal of this rejection.

Nevertheless, Applicants have enclosed herewith a Second Substitute Sequence Listing in paper and computer readable form to add these pentapeptides as SEQ ID NOS:99-101. The enclosed Second Substitute Sequence Listing also includes the *Saccharomyces cerevisiae* sequences depicted in Figures 5 and 10 as SEQ ID NOS:102 and 103, respectively. I hereby state that the content of the paper and computer readable copies of the Substitute Sequence Listing submitted in accordance with 37 C.F.R. §1.821(c) and (e), are the same. I hereby state that the content of the paper and computer readable copies of the Substitute Sequence Listing, submitted in accordance with 37 C.F.R. §1.821(g), herein does not include new matter.

## **II. Amended Abstract Complies with Requirements**

The Examiner has objected to the form of the abstract of the instant application for failing to be printed on a separate sheet. In response, Applicants enclose herewith an amended Abstract on a separate sheet. The amended Abstract is supported by the Abstract of International Application PCT/EP98/06977 of which the instant application is a National Stage Application under 35 U.S.C. §371. Applicants believe that the amended Abstract complies with 37 C.F.R. §1.52(b)(4) and, therefore, respectfully request withdrawal of this rejection.

## **III. Claims Are Free of Objections**

The Examiner has objected to claims 3, 11, and 29-33 as allegedly either depending on non-elected claims or reciting non-elected subject matter. This objection is moot with respect to 11 and 31 since these claims have been cancelled. Applicants assert that the remaining claims, namely claims 3, 29-30, and 32-33, have been amended to overcome this objection.

The Examiner has objected to claim 29 under 37 C.F.R. §1.75(c) as allegedly being in improper form. Amended claim 29 recites only claim 13 and, therefore, fully complies with 37 C.F.R. §1.75(c).

Therefore, Applicants, respectfully request withdrawal of these objections.

**IV. Claims Comply with 35 U.S.C. §112, second paragraph**

Claims 1-3, 7-23, and 29-33 have been rejected under 35 U.S.C. §112, second paragraph as indefinite for allegedly failing to particularly point out and distinctly claim the subject matter that the Applicant regards as the invention.

Claims 2, 3, 8-12, 14-23, and 29-33 have been rejected as allegedly indefinite for reciting the article "a" instead of the article "the". Claims 2, 11, and 31 have been cancelled rendering this rejection moot as to these claims. Claims 3, 8-10, 12, 14-23, 29-30, and 32-33 have been amended to recite the article "the". Applicants, therefore respectfully request withdrawal of this rejection.

Claims 2, 3, 7, 8, 11, and 13 have also been rejected as allegedly indefinite for reciting the term "homologous". The Examiner has alleged that the art uses this term as a qualitative means of comparing two sequences. Claims 2, 7, and 11 have been cancelled rendering this rejection moot as to these claims. Claims 3, 8, and 13 have been amended to recite identity, instead of homology. This amendment is fully supported by the application as filed as set forth on pages 13-14, above. Applicants assert that the artisan of ordinary skill would recognize that identity is a quantitative means of comparing the relatedness of two sequences. Applicants, therefore respectfully request withdrawal of this rejection.

Claims 7-10, 12-13, 15, 21-23, and 29 have been rejected as allegedly indefinite for reciting "capable" or "causing", which the Examiner has alleged does not denote a positive or

definite property, but merely a suggested function. Claim 7 has been cancelled rendering this rejection moot as to this claim. Amended claims 8-10, 12-13, 15, 21-23, and 29 do not recite "capable" or "causing". Applicants, therefore respectfully request withdrawal of this rejection.

Claim 12 has been rejected as allegedly unclear as to how the regulation element is operably linked to the DNA molecule. Since amended claim 12 recites "a regulation element operably linked to the nucleotide sequence...", Applicants respectfully request withdrawal of this rejection.

In addition, claims 14 and 20 have been rejected as indefinite for allegedly being in improper Markush format. Applicants assert that claims 14 and 20 as amended fully comply with MPEP §2173.05(h) and, therefore respectfully request withdrawal of this rejection.

Lastly, claims 21-23 have been rejected as indefinite for allegedly failing to recite an essential step. Applicants assert that claims 21-23 as amended do not omit any essential steps and, therefore respectfully request withdrawal of this rejection.

**V. Claims Comply with 35 U.S.C. §112, first paragraph**

**A. Claims Are Supported by an Adequate Written Description**

Claims 1-3, 7-23, and 29-33 have been rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter that was not described in the specification in such a way as to convey to one of ordinary skill in the art that Applicants had possession of the invention at the time the application was filed. The Examiner has alleged that Applicants disclose only one sequence, SEQ ID NO:19, within the elected invention that is functionally involved in a mismatch repair system. The Examiner has alleged that it is insufficient to define a chemical compound solely by its principle biological property.

Applicants traverse this rejection and assert that the artisan of ordinary skill would recognize that Applicants were in possession of the claimed invention at the time the application was filed. Claims 1, 2, 7, 11, and 31 have been cancelled rendering this rejection moot as to these claims. Claims 8-10, 12 and 21 are dependent on independent claim 3. Claims 14-20, 22-23, 29-30, and 32-33 are dependent on independent claim 13. Claims 39-44 are dependent on claim 38. This rejection will be addressed primarily with respect to independent claims 3, 13, 37, and 38.

Claims 3, 37, and 38 do not recite function. The artisan of ordinary skill would recognize that Applicants had possession of at least nucleic acids within the scope of claim 37 at the time the application was filed in view of SEQ ID NOS:18 and 19. In addition, the artisan of ordinary skill would recognize that Applicants had possession of nucleic acids within the scope of claims 3 and 38 at the time the application was filed in view of the disclosures, *inter alia*, at page 8, lines 13-16, page 14, lines 29-33, and Figure 5. Claim 13 uses the same 50% identity language as claim 3, but adds functional limitations. Therefore, the functional limitations of claim 13 do not constitute the sole definition of the claimed nucleic acid. Applicants, therefore, respectfully request withdrawal of this rejection.

B. Claims Are Fully Enabled

Claims 1-3, 7-23, and 29-33 have been rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in such a way as to enable one skilled in the art to make and/or use the invention. The Examiner has alleged that the specification is not enabling for any isolated DNA molecule that encodes a polypeptide functionally involved in the DNA mismatch repair system of a plant.

Applicants traverse this rejection and assert that all pending claims are fully enabled by the specification and that the Examiner has not satisfied the burden imposed by MPEP §2164.04 to make this rejection.

The Examiner has acknowledged that the specification is enabling for an isolated DNA molecule that encodes a polypeptide having the sequence of SEQ ID NO:19, compositions comprising said isolated DNA molecule, and methods of using said DNA molecule in *Arabidopsis thaliana*. See Paper 16, Office Action dated May 21, 2002, page 11, lines 17-20. In view of this acknowledgement, Applicants respectfully invite the Examiner's attention to claims 38-44 and assert that these claims are in condition for allowance.

The Examiner has acknowledged that the instant specification provides general guidance how to isolate similar proteins based on conserved sequences in human and yeast analogues. See Paper 16, Office Action dated May 21, 2002, page 13, lines 5-9. However, the Examiner has alleged that the specification does not teach how to recognize all polypeptides functionally involved in the DNA mismatch repair system of a plant.

Applicants respectfully invite the Examiner's attention to pending independent claims 3, 13, and 37, which do not recite functional involvement in DNA mismatch repair. Instead, claims 3, 13, and 37 recite 50% identity to SEQ ID NO:19. Applicants assert that one of ordinary skill in the art would recognize that plant mismatch repair proteins are highly conserved. See e.g. Cao X et al., 2000, "Conserved plant genes with similarity to mammalian de novo DNA methyltransferases" *Proc Natl Acad Sci USA* 97(9):4979-4984; Xu H et al., 1998, "Plant homologue of human excision repair gene ERCC1 points to conservation of DNA repair mechanisms" *Plant J.* 13(6):823-9; and Tuteja N et al., 2001, "Molecular mechanisms of DNA damage and repair: progress in plants" *Crit. Rev. Biochem Mol. Biol.* 36(4):337-397. Thus, in

view of the high degree of conservation of mismatch repair proteins, the guidance provided in the instant specification together with the 50% identity recitation of the claims is sufficient to allow the artisan of ordinary skill to recognize all nucleic acids within the scope of the claims. Therefore, Applicants respectfully request withdrawal of these rejections.

In rejecting claims 21-23 and 29-33, the Examiner has alleged that regulation of plant genes by antisense technology is unpredictable and has cited Colliver SP et al., 1997, *Plant Mol. Biol.* 35:509-522 (hereinafter "Colliver") to support this allegation.

Applicants traverse this rejection and assert that the Examiner has not satisfied the burden imposed under MPEP §2164.04 to establish a reasonable basis for unpredictability where the literature is replete with examples of effective use of antisense technology to regulate target gene expression in plants. Colliver discloses the results of antisense expression of a chalcone synthase gene in *Lotus corniculatus*, a member of the family Fabaceae. Applicants respectfully invite the Examiner's attention to documents 1-5, 7, 10-12 and 14-27 cited on the Supplemental Information Disclosure Statement enclosed herewith. These documents disclose the effective use of antisense technology to regulate a wide variety of genes in plants such as arabidopsis, tomato, tobacco, soybean, maize, rice, potato, barley, and bird's foot trefoil. Applicants respectfully invite the Examiner's particular attention to documents 19, 21, and 23, which disclose, effective, predictable use of antisense technology in *Lotus corniculatus*, and documents 17 and 18, which disclose, effective, predictable use of antisense technology to regulate DNA repair genes.

The standard for predictability to support enablement is not absolute predictability, but rather a balance of predictability with the amount of detail provided in the disclosure. *See e.g.* MPEP §2164.03. Thus, while IDS documents 1-6, 8, 10-26 may not



demonstrate absolute predictability, they clearly establish that a substantial degree of predictability exists. In view of these documents, Applicants assert that the Examiner's citation of a single document where the results in an esoteric species were not as predicted, fails to satisfy the burden imposed by MPEP §2164.04 to establish a reasonable basis for requiring Applicants to demonstrate actual reduction to practice. On the contrary, the disclosures of, *inter alia*, Example 3 are sufficient to enable the artisan of ordinary skill in the art to practice the full scope of the claimed invention. Therefore, Applicants respectfully request withdrawal of this rejection.

## **VI. Rejections Under 35 U.S.C. §102**

### **A. Claims Are Not Anticipated by Culligan**

Claims 1-3 and 7-11 have been rejected under 35 U.S.C. 102(a) as allegedly anticipated by Culligan et al., 1997, *Plant Physiology* 115(2):833-839 (hereinafter "Culligan"). The Examiner has alleged that Culligan discloses an isolated DNA molecule encoding atMSH2, which is functionally involved in the DNA mismatch repair system of a plant and "homologous" to SEQ ID NO:19.

Applicants traverse this rejection and assert that Culligan is not available as prior art against the instant invention. Applicants respectfully invite the Examiner's attention to the filing date of Applicant's Australian application PO9745, namely **October 10, 1997**, to which the instant application claims priority. Culligan was published in the October 1997 issue of *Plant Physiology*. See Culligan, p. 833, header. Applicant's respectfully invite the Examiner's attention to an electronic letter from the Production Manager of *Plant Physiology* that indicates that the publication date of the October 1997 issue was **October 14, 1997**. This date is four days **after** Applicants priority date of **October 10, 1997**.

The sequences disclosed in Culligan have been deposited in GenBank and assigned accession numbers AF002706, AF009657, and AF003005. Applicants respectfully invite the Examiner's attention to the attached information obtained from the National Center for Biotechnology Information (NCBI) Sequence Revision History internet site at <http://www.ncbi.nlm.nih.gov/entrez/sutils/girevhist.cgi> regarding the Culligan sequences. According to NCBI, these sequences were first deposited on **October 15, 1997**. This date is also after Applicants priority date of **October 10, 1997**.

Applicants next respectfully invite the Examiner's attention to the attached information regarding Culligan obtained from the National Center for Biotechnology Information PubMed internet site at <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi>. According to the printed information, Culligan was first indexed for PubMed and Medline databases on **October 29, 1997**. This date is after Applicants priority date of **October 10, 1997**.

Applicants assert that, in view of the foregoing information, Culligan is not available as prior art against the instant invention. Alternatively, the foregoing information at least indicates that the Examiner has not satisfied the burden of showing that Culligan is available as prior art pursuant to MPEP §§ 706.02(a) and 2128.

Since Culligan is not available as prior art based on its publication date, Applicants respectfully request withdrawal of this rejection.

B. Claims Are Not Anticipated by Michiels

Claims 1, 2, 7-10, 12-23, and 29-33 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Michiels et al., PCT Publication No. WO 96/26283 (hereinafter "Michiels"). The Examiner has alleged that Michiels discloses an isolated DNA molecule encoding the ribozyme barnase, which the Examiner has alleged is "functionally involved in the

DNA mismatch repair system of a plant. *See* Paper 16, Office Action dated May 21, 2002, page 16, lines 5-9. The Examiner further has alleged that Michiels discloses chimeric genes and plasmids comprising this DNA, as well as a process for partially inactivating the DNA mismatch repairs system of a plant.

Applicants traverse this rejection and assert that Michiels fails to teach each and every element of the instant claims as amended. Specifically, Michiels fails to teach a nucleic acid encoding an amino sequence either having the sequence of SEQ ID NO:19 or a sequence 50% identical to SEQ ID NO:19. Applicants respectfully invite the Examiner's attention to Sequence Alignments 1-4 attached hereto. These alignments were performed using the ClustalW (1.74) algorithm as provided at <http://www.ch.embnet.org/software/ClustalW.html> with default settings. Positions where both sequences have identical amino acids are marked with asterisks and percent identity was calculated according to the foregoing formula (I).

The protein encoded by the complement of Michiels SEQ ID NO:1, nucleotides 2284-2624, displays the highest percent identity to SEQ ID NO:19 of the instant invention with 2.1%. However, this is far below the 50% identity figure recited by the instant claims. Therefore, Michiels fails to teach every each and every element of the claimed invention.

Since Michiels fails to teach each and every element of the invention, Applicants respectfully request withdrawal of this rejection.

#### **VI. Rejections Under 35 U.S.C. §103**

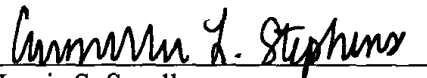
Claims 12-20 have been rejected under 35 U.S.C. 103(a) as allegedly obvious in view of Culligan. The Examiner has alleged that it would have been obvious to one of ordinary skill in the art to attach a regulation control sequence to the sequence of Culligan.

Applicants traverse this rejection and assert that Culligan is not available as prior art against the instant invention since it was published after Applicants priority date as discussed in preceding section VI.A. Therefore, Applicants respectfully request withdrawal of this rejection.

Applicants have enclosed the fee for a one-month extension of time as required under 37 C.F.R. §1.17(a)(1). Applicants have also enclosed the fee under 37 C.F.R. §1.17(p) for submitting an Information Disclosure Statement pursuant to 37 C.F.R. §1.97(c). Applicants do not believe any additional fee is required for this filing. Nevertheless, the Commissioner is hereby authorized to charge any fees required for this submission not otherwise enclosed herewith to Deposit Account No. 02-4377. Two copies of this page are enclosed.

Respectfully submitted,

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Enclosures



VERSION WITH MARKINGS TO SHOW CHANGES MADE

This marked-up version was prepared with DeltaView software (v2.5.163). In this section, added text is marked with double underlining. e.g. added text, and deleted text is marked by a single strikethrough, e.g. ~~deleted text~~.

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IN THE CLAIMS

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Claim 3 has been amended as follows:

3. (AMENDED) ~~A DNA molecule according to claim 1 wherein~~  
~~said~~An isolated and purified nucleic acid comprising a  
nucleotide sequence encoding a polypeptide having an amino  
acid sequence that is homologous at least 50% identical to  
the amino acid sequence of the Arabidopsis thaliana Mts  
homolog 3 protein (AtMSH3) (SEQ ID NO: 19) or to AtMSH6 (SEQ  
ID NO: 31).

Claim 8 has been amended as follows:

8. (AMENDED) ~~A DNA molecule~~The nucleic acid according to  
claim ~~7~~ comprising a3, wherein said polynucleotide ~~sequence~~  
~~encoding a polynucleotide capable of interfering~~interferes  
with the expression of a plant polynucleotide sequence  
encoding a polypeptide ~~which is homologous~~having at least  
50% amino acid identity to a mismatch repair polypeptide of

~~a yeast or of a human~~AtMSH3 (SEQ ID NO:19) and thereby  
~~disabling~~disables said plant polynucleotide sequence.

Claim 9 has been amended as follows:

9. (AMENDED) ~~A DNA molecule~~The nucleic acid according to claim 8 wherein said polynucleotide ~~is capable of interfering~~interferes with the expression of a plant polynucleotide sequence is a sense polynucleotide, an antisense polynucleotide or a ribozyme.

Claim 10 has been amended as follows:

10. (AMENDED) ~~A DNA molecule~~The nucleic acid according to claim 7 ~~comprising a polynucleotide sequence encoding a3 wherein said polypeptide capable of disrupting~~disrupts the DNA mismatch repair system of a plant.

Claim 12 has been amended as follows:

12. (AMENDED) ~~A DNA molecule~~The nucleic acid according to claim 10 further comprising a regulation element ~~capable of causing~~operably linked to the nucleotide sequence encoding said polypeptide, wherein said regulation element causes overexpression of said polypeptide in a cell of said plant.

Claim 13 has been amended as follows:

13. (AMENDED) A chimeric gene comprising:  
a ~~DNA~~nucleic acid sequence selected from the group  
consisting of (i) a nucleotide sequence ~~encoding a~~  
~~polynucleotide capable of interfering with the expression~~  
~~of a plant polynucleotide sequence encoding a polypeptide~~  
~~which is homologous~~having at least 50% identity to a  
~~mismatch repair polypeptide of a yeast or of a human and~~  
~~thereby disabling said plant polynucleotide sequence,~~SEQ ID  
NO:18, and (ii) a nucleotide sequence encoding a  
~~polypeptide capable of disrupting the DNA mismatch repair~~  
~~system of a plant~~having at least 50% identity to AtMSH3  
(SEQ ID NO:19); and at least one regulation element ~~capable~~  
~~of functioning in a plant cell~~operably linked to said  
nucleic acid sequence.

Claim 14 has been amended as follows:

14. (AMENDED) ~~A~~The chimeric gene according to claim ~~13~~13,  
wherein said regulation element is selected from the group  
consisting of constitutive, inducible, tissue type specific  
and cell type specific promoters.

Claim 15 has been amended as follows:

15. (AMENDED) ~~A~~The chimeric gene according to claim ~~13~~  
~~comprising a DNA sequence encoding a polypeptide capable of~~  
~~disrupting the DNA mismatch repair system of a plant, 13,~~  
wherein said nucleic acid sequence is (ii) an AtMSH3-  
encoding sequence, said regulation element ~~is capable of~~  
~~causing~~causes overexpression of said polypeptide sequence in  
a cell of said plant, and said polypeptide disrupts the DNA  
mismatch repair system of a plant.

Claim 16 has been amended as follows:

16. (AMENDED) ~~A~~The chimeric gene according to claim 13 wherein  
said regulation element is selected from the group  
consisting of 35S, NOS, PR1a, AoPR1 and DMC1.

Claim 17 has been amended as follows:

17. (AMENDED) A plasmid or vector comprising ~~a~~the chimeric gene  
according to any one of claims 13-16.

Claim 18 has been amended as follows:

18. (AMENDED) A plant cell stably transformed, transfected or  
electroporated with ~~a~~the plasmid or vector according to  
claim 17.



Claim 19 has been amended as follows:

19. (AMENDED) A plant comprising athe cell according to claim 18.

Claim 20 has been amended as follows:

20. (AMENDED) AThe plant according to claim ~~19~~19, wherein said plant is selected ~~from plants of the families~~group consisting of Brassicaceae, Poaceae, Solanaceae, Asteraceae, Malvaceae, Fabaceae, Linaceae, Canabinaceae, Dauaceae and Cucurbitaceae.

Claim 21 has been amended as follows:

21. (AMENDED) A process for at least partially inactivating athe DNA mismatch repair system of a plant cell, comprising: transforming or transfecting said plant cell with a DNA~~nucleic molecule~~acid according to any one of claims ~~13, 8-310, or 7-12 and causing~~12, growing said DNA~~cell~~ under conditions that permit expression of said nucleic acid sequence to express, and inactivating said polynucleotide ~~or~~DNA mismatch repair system of said polypeptideplant cell.

Claim 22 has been amended as follows:

22. (AMENDED) A process for at least partially inactivating a DNA mismatch repair system of a plant cell, comprising: transforming or transfecting said plant cell with a chimeric gene according to any one of claims 13-16 and causing 16, growing said DNA sequence to express cell under conditions that permit expression of said polynucleotide or, and inactivating said polypeptide DNA mismatch repair system of said plant cell.

Claim 23 has been amended as follows:

23. (AMENDED) A process for at least partially inactivating a DNA mismatch repair system of a plant cell, comprising: transforming or transfecting said plant cell with a plasmid or vector according to claim 17 and causing 17, growing said DNA sequence to express cell under conditions that permit expression of said polynucleotide or, and inactivating said polypeptide DNA mismatch repair system of said plant cell.

Claim 29 has been amended as follows:

29. (AMENDED) A process ~~according to claim 28 wherein said step~~ effor altering the DNA mismatch repair system ~~comprises~~ introducing into a plant or plant cell comprising:

~~transforming or transfecting said hybrid plant, plant, plant~~  
~~or plant cell or cells a chimeric gene according to claim 13~~  
~~and permitting the chimeric gene to express a polynucleotide~~  
~~which is capable of interfering with the chimeric gene of~~  
~~claim 13, growing said plant or plant cell under conditions~~  
~~that permit expression of a plant polynucleotidesaid nucleic~~  
~~acid sequence in a mismatch repair gene of the hybrid plant,~~  
~~plant, cell or cells, or a polypeptide capable of disrupting~~  
~~theand altering said DNA mismatch repair system of the~~  
~~hybridsaid plant, cell or cells.~~

Claim 30 has been amended as follows:

30. (AMENDED) ~~A~~The process according to claim 29 ~~comprising~~29,  
wherein said altering comprises inactivating an ~~MSH1~~MSH3  
gene ~~and/or an MSH6 gene of said plant cell.~~

Claim 32 has been amended as follows:

32. (AMENDED) ~~A~~The process according to claim 28 ~~comprising at~~  
~~least partially inactivating the mismatch repair system~~  
~~of~~29, wherein said plant cell is in a plant and has a  
predetermined cell type or is in a predetermined tissue of  
~~said~~a plant, and wherein said altering the mismatch repair

system consists of at least partially inactivating said mismatch repair system.

Claim 33 has been amended as follows:

33. (AMENDED) ~~A~~The process according to claim 32 further comprising restoring mismatch repair in<sup>29</sup>, wherein said plant cell is in a plant and has a predetermined cell type or said is in a predetermined tissue of a plant, and wherein said altering the mismatch repair system consists of enhancing mismatch repair in said cell.

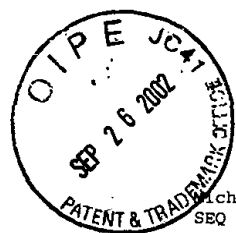
#### IN THE SPECIFICATION

The abstract has been amended as follows:

(AMENDED) ~~An~~The present invention relates to an isolated and purified DNA molecule comprising a polynucleotide<sup>sequence encoding that encodes</sup> a polypeptide functionally involved in the DNA mismatch repair system of a plant.

The paragraph beginning at page 12, line 34 and ending at page 13, line 4 has been amended as follows:

(AMENDED) Primers UPMU and DOMU correspond to conserve amino acid sequences of the proteins MutS (*E. coli* and *S. typhimurium*), HexA (*S. pneumoniae*), Repl (mouse) and Ducl (human). The conserved regions to which they are targeted are TGPNM (SEQ ID NO:99) for UPMU ~~(amino acid positions 852-856 for AtMSH6 and 816-820 for AtMSH3)~~ FATHY (SEQ ID NO:100) or FVTHY (SEQ ID NO:101) for DOMU ~~(amino acid positions 964-968 for AtMSH6 and 928-932 for AtMSH3, respectively.)~~ These primers have been used to isolate MSH2 and MSH 1 from yeast (Reenan and Kolodner, Genetics 132:963-973 (1992)) and MSH2 from *Xenopus* and mouse (Varlet et al., Nuc. Acids Res. 22:5723-5728 (1994)).



# ALIGNMENT 1

Part of  
Paper # 19/0  
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Michiels 1  
SEQ ID NO:19  
-----  
MKGKQQTISRFFAPKPKSPTHEPNVAESSTPPPKISATVSFSPSKRKLSDHLAAASP

Michiels 1  
SEQ ID NO:19  
-----  
KKPKLSPHTQNPVDPNLHQRFLEPSPEEYVPETSSSRKYTPLEQQVVELKSKYPD

Michiels 1  
SEQ ID NO:19  
-----  
VVLMEVGYYRFFGEDAEIAARVLGIYAHMDHNFMTASVPTFRLNPHVRRLLVNAGYKIG

Michiels 1  
SEQ ID NO:19  
-----  
VVKQTETAAIKSHGANRTGPFPRGLSALYTKATLEAAEDISGGCGGEEGFGSQSNFLVCV

Michiels 1  
SEQ ID NO:19  
-----  
VDERVKSETLGCGLIEMSFDRVGVVGVEISTGEVVYEEFNDNFMRSGLEAVILSLSPAEL

Michiels 1  
SEQ ID NO:19  
-----  
LLGQPLSQQTEKFLVAMAGPTSNVRVERASLDCFSNGNAVDEVISLCEKISAGNLEDDKE

Michiels 1  
SEQ ID NO:19  
-----  
MKLEAAEKGMSCLTVHTIMNMPHLTVQALALTFCCLKQFGFERILYQGASFRSLSNTEM

Michiels 1  
SEQ ID NO:19  
-----  
TLSANTLQOLEVVKNNSDGSSEGLFHNMTHTLVYGSRLLRHWTHPLCDRLISARLD

Michiels 1  
SEQ ID NO:19  
-----  
AVSEISACMGSHSSSQLSSELVEEGSERAIVSPEFYLVLSSVLTAMSRSSDIQRGITRIF

Michiels 1  
SEQ ID NO:19  
-----  
HRTAKATEFIAVMEAILLAGKQIQRLGIKQDSEMRSMQSATVRSTLLRKLISVISSPVVV

Michiels 1  
SEQ ID NO:19  
-----  
-----MVPVINTFDGVA-DYLQTYHKLPDNYITKSEA-QALGWVASKGN--LADVAPGKS  
DNAGKLLSALNKEAAVRGDLDDILITSSDQFPELAEARQAVLVIREKLDSSIASFRKKLA  
\* \* \* \* \*

Michiels 1  
SEQ ID NO:19  
-----  
IGGDIFSNREGK-----LPGKSGR--TWREADINYTSGFRNSDRILYSSDWLIYKTTDHY  
IRNLEFLQVSGITHLIELPVDKVPVHNWVKVNSTKKTIRYHPPEIVAGLDELALAT-EHL  
\* \* \* \* \*

Michiels 1  
SEQ ID NO:19  
-----  
QTFTKIRG-----  
AIVNRASWDSPLKSFSTRYYTDFKAAVQALALDCLHSLSTLSRNKNYVRPEFVDDCEPVE

Michiels 1  
SEQ ID NO:19  
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INIQSGRHPVLETILQDNFVFNPTILHAEGEYQIITGPNMGGKSCYIRQVALISIMAQV

Michiels 1  
SEQ ID NO:19  
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GSFVPASFAKLHVLDGVFTRMGASDSIQHGRSTFLEELSEASHIIRTCSSRLVILDELG

Michiels 1  
SEQ ID NO:19  
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RGTSTHDGVAIAYATLQHLAELKRLVLFVTRYPEIAEISNGFPGSVGTYHVSYLTLQKD

Michiels 1  
SEQ ID NO:19  
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KGSYDHDVTVLYKLVRGLCSRSPGPKVAQLAQPSCIRRAISMAAKLEAEVRERERT

Michiels 1  
SEQ ID NO:19  
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RMGEPEGHEEPRGAEESISALGDLFADLKPFALSEEDPWKAFLKHWKIAGKIRLKPTC

Michiels 1  
SEQ ID NO:19  
--  
SF

Percent Identity =  $\frac{23}{1082} \times 100$

Percent Identity = 2.1%

## ALIGNMENT 2

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Michiels 2 -----
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Michiels 2 -----
SEQ ID NO:19 KKPKLSPHTQNPVDPNHLQRFQRFLEPSPPEYVPEPSSSRKYTPLEQQVVELKSKYPD

Michiels 2 -----
SEQ ID NO:19 VVLMVEVGYYRFFGEDAEIAARVLGIYAHMDHNFMTASVPTFRLNFHVRRLVNAGYKIG

Michiels 2 -----
SEQ ID NO:19 VVKQTETAAIKSHGANRTGPFGRGLSALYTKATLEAAEDISGGCGGEGFGSQSNFLVCV

Michiels 2 -----
SEQ ID NO:19 VDERVKSETLGCGLIEMSFVVRVGVGVVEISTGEVVYEEFNDFMRSGLEAVILSLSPAEL

Michiels 2 -----
SEQ ID NO:19 LLGQPLSQQTEKFLVAMAGPTSNVRVERASLDCFSNGNAVDEVISLCEKISAGNLEDDKE

Michiels 2 -----MK
SEQ ID NO:19 MKLEAAEKGMCLTVHTIMNMPHLTVQALALTFCHLKQGFGERILYQGASFRSLSSNTEM

Michiels 2 -----
SEQ ID NO:19 KAVINGEQIRSIIDLHQTLKKELALPEYYGENLDALWDCLT-GWVEYPLVLEWRQFEQSK
TISANTLQQLEVVKNNSDGSESGSLFHNMNHTLTVYGSRLLRHWVTHPLCDRNLI SARLD
      *      *      *      *      *      *      *      *

Michiels 2 -----
SEQ ID NO:19 QLTEN---GAESVLQVFREKAEGCDITIILS-----
AVSEISACMGSHSSQLSSELVEEGSERAIVSPEFYLVLSVLTAMSRSSDIQRGITRIF
      *      *      *      *      *      *      *

Michiels 2 -----
SEQ ID NO:19 HRTAKATEFIIVMEAILLAGKQIQRLGIKQDSEMRSMQSATVRSTLLRKLISVISSPVVV

Michiels 2 -----
SEQ ID NO:19 DNAGLLSALNKEAAVRGDLILDITSSDQFPELAEARQAVLVIREKLDSSIASFRKKLA

Michiels 2 -----
SEQ ID NO:19 IRNLEFLQVSGITHLIELPVDSKVPHNWVKVNSTKKTIRYHPPEIVAGLDELALATEHLA

Michiels 2 -----
SEQ ID NO:19 IVNRASWDSFLKSFRIYTDFAAVQALAAALDCLHSLSTLSRNKNYVRPEFVDDCEPVEI

Michiels 2 -----
SEQ ID NO:19 NIQSGRHPVLETILQDNFVFNDTILHAEGEYCQIITGPNMGGKSCYIRQVALISIMAVG

Michiels 2 -----
SEQ ID NO:19 SFVPASFAKLHVLDGVFTRMGASDSIQHGRSTFLEELSEASHIIRTCSRSLVILDELGR

Michiels 2 -----
SEQ ID NO:19 GTSTHDGVAIAYATLQHLAELKRCVLFVTHYPEIAEISNGFPGSVGTYHVSYLTLQKDK

Michiels 2 -----
SEQ ID NO:19 GSYDHHDDTYLYKLVRGLCSRSFGFKVAQLAQIPPCIRRAISMAAKLEAEVRARERNT

Michiels 2 -----
SEQ ID NO:19 MGEPEGHEEPGAESISALGDLFADLKFALSEEDPWKAPEFLKHAWKIAGKIRLKPTCS

Michiels 2 -----
SEQ ID NO:19 -
F

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$$\text{Percent Identity} = \frac{17}{1081} * 100$$

$$\text{Percent Identity} = 1.6\%$$

### ALIGNMENT 3

```

Michiels 3 -----
SEQ ID NO:19  MGKQKQQTISRFFAPKPKSPTHEPNPVAESSTPPPKISATVSFSPSKRKLLSDHLAAASP

Michiels 3 -----
SEQ ID NO:19  KKPKLSPHTQNPVPDPNLHQRFLEPSPEEYVPETSSSRKYTPLEQQVVELKSKYPD

Michiels 3 -----
SEQ ID NO:19  VVLMVEVGYYRFFGEDAEIAARVLGIYAHMDHNFMTASVPTFRLNFHVRRLVNAGYKIG

Michiels 3 -----
SEQ ID NO:19  VVKQTETAAIKSHGANRTGPFPRGLSALYTKATLEAAEDISGGCGGEGFGSQSNFLVCV

Michiels 3 -----
SEQ ID NO:19  VDERVKSETLGCIGIEMSPDVRVGVGVEISTGEVVYEEFNDNFMRSGLAIVLSLSPAEL

Michiels 3 -----
SEQ ID NO:19  LLGQPLSQQTEKFLVAMAGPTSNVRVERASLDCFSNGNAVDEVISLCEKISAGNLEDDKE

Michiels 3 -----
SEQ ID NO:19  MKLEAAEKGMSCLTVHTIMNMPHLTVQALALTFCHLKQFGFERILYQGASFRLSSNTEM

Michiels 3 -----
SEQ ID NO:19  TLSANTLQQLLEVVKVNSDGSSESGSLFHNWHTLTVYGSRLLRHWVTHPLCDRNLI SARLD

Michiels 3 -----
SEQ ID NO:19  AVSEISACMGSHSSSQLSSELVEEGSERAIVSPEFYVLVSSVLTAMSRSDIQRGITRIF

Michiels 3 -----
SEQ ID NO:19  HRTAKATEFIAVMEAILLAGKQIQRLGIKQDSEMRSMQSATVRSTLLRKLISVISSPVVV

Michiels 3 -----
SEQ ID NO:19  DNAGKLLSALNKEAAVRGDLDDILITSSDQFPELAEARQAVLVIREKLDSSIASPRKLA

Michiels 3 -----
SEQ ID NO:19  IRNLEFLQVSGITHLIELPVDKVPVHNWVKNSTKKTIRYHPPEIVAGLDELALATEHLA

Michiels 3 -----
SEQ ID NO:19  IVNRASWDSFLKSFSSRYTDFKAAVQALAAALDCLHSLSTLSRNKNYVRPEFVDDCEPVEI

Michiels 3 -----MVPVINTFDGVADYLQTYHKL PDNYITKSEAQALGWVASKGNL
SEQ ID NO:19  NQSGRHPVLETLQDNFVPNDTILHAEGEYCIIITG-PNMGKSCYIRQVALISIMAVV
                **          * *          *

Michiels 3  ADVAPG---KSIGGDIFSNREGK-LPGKSGR-TWREADINYTSGFR-NSDRILYSSDWLI
SEQ ID NO:19  GSFVPASFAKLHVLDGVFTRMGASDSIQHGRSTFLEELSEASHIIRTCSSRLVILDELG
                *   *   *   *   *   *   *   *   *   *   *   *

Michiels 3  YKTTDHYQTFTKIR-----
SEQ ID NO:19  RGTSTHDGVAIAYATLQHLAEKRCCLVLFVTHYPEIAEISNGFPGSVGTYHVSYLTLQKD
                *   *

Michiels 3 -----
SEQ ID NO:19  KGSYDHDDVTYLYKLVRGLCSRSFGFKVAQLAQIPPCIRRAISMAAKLEAEVRARERT

Michiels 3 -----
SEQ ID NO:19  RMGEPEGHEEPRGAEEISALGDLFADLKPALSEEDPWKAPEFLKHAWKIAGKIRLKPTC

Michiels 3  --
SEQ ID NO:19  SF

```

$$\text{Percent Identity} = \frac{22}{1082} * 100$$

Percent Identity = 2.0%



# ALIGNMENT 4

```

Michiels 4 -----
SEQ ID NO:19 MGKQKQQTISRFFAPKPKSPTHEPNPVAESSTPPPKISATVSFSPSKRKLSDHLAAASP

Michiels 4 -----
SEQ ID NO:19 KKPKLSPHTQNPVPDNLHQRFLQRFLEPSPEEYVPETSSSRKYTPLEQQVVELKSKYPD

Michiels 4 -----
SEQ ID NO:19 VVLMVEVGYRFRFFGEDAEIAARVLGIYAHMDHNFMTASVPTFRLNPHVRRLVNAGYKIG

Michiels 4 -----
SEQ ID NO:19 VVKQTETAAIKSHGANRTGPPFRGLSALYTKATLEAAEDISGGCGGREGFGSQSNPLVCV

Michiels 4 -----
SEQ ID NO:19 VDERVKSETLGCGIEMSPDVRVGUVGVEISTGEVVYEEFNDNFMRSGLAVILSLSPAEL

Michiels 4 -----
SEQ ID NO:19 LLGQPLSQQTEKFLVAMAGPTSNVRVERASLDGFSNGNAVDEVISLCEKISAGNLEDDKE

Michiels 4 -----
SEQ ID NO:19 MKLEAAEKGMSCLTVHTIMNMPHLTVQALALTFCHLKQFGFERILYQGASFRSLSSNTEM

Michiels 4 -----
SEQ ID NO:19 TLSANTLQQLEVVKNNSDGSESGSLFHNMTHTLVYGSRLLRHWVTHPLCDRNLI SARLD

Michiels 4 -----
SEQ ID NO:19 AVSEISACMGSHTSSQLSSELVEEGSERAIVSPEFYLVLSVLTAMSRSSDIQRGITRIF

Michiels 4 -----
SEQ ID NO:19 HRTAKATEFIAVMEAILLAGKQIQRLGKQDSEMRSMQSATVRSTLLKRLISVISFVVV

Michiels 4 -----
SEQ ID NO:19 DNAGKLLSALNKEAAVRGDLDLITSSDQPELAEARQAVLVIREKLDSSIASFRKKLA

Michiels 4 -----
SEQ ID NO:19 IRLNLEFLQVSGITHLIELPVDGSKVPHNWKVNSTKKTIRYHPPEIVAGLDELALATEHLA

Michiels 4 -----
SEQ ID NO:19 IVNRASWDSFLKSFSRYTDFKAAVQALAAALDCLHSLSTLSRNKNYVRPEFVDDCEPVEI

Michiels 4 -----MVPVINTFDGVADYVQTYHKLDPDNYITKSEAQALGWVASKGNL
SEQ ID NO:19 NIQSGRHPVLETLIQDNFVPNDTILHABGEYCQIITG-PNMGKSCYIRQVALISIMAVQ
                **      * *      *

Michiels 4 ADVAPG---KSIIGDIFSREGK-LPGKSGR-TWREADINYTSGFR-NSDRILYSSDWLI
SEQ ID NO:19 GSFVPASFAKLHVLDGVFTRMGASDSIQHGRSTFLEELSEASHIIRTCSRSLVILDELG
                * *      * *      * *      * *      * *      * *

Michiels 4 YKTTDHYQTFTKIR-----
SEQ ID NO:19 RGTSTHDGVAIAYATLQHLAEKRCLVLFVTHYPEIAEISNGFPGSVGTYHVSYLTLQKD
                * *

Michiels 4 -----
SEQ ID NO:19 KGSYDHDVITYLYKLVRGLCSRSFGFKVAQLAQIPPCIRRAISMAAKLEAEVRERNT

Michiels 4 -----
SEQ ID NO:19 RMGEPGHEEPGAEESISALGDLFADLKFALSEEDPWKAFEFLKAWKIAGKIRLKPTC

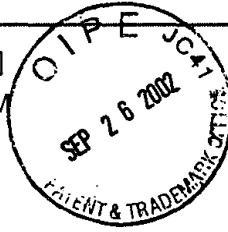
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SEQ ID NO:19 SF

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22  
 Percent Identity = ----- \* 100  
 1082

Percent Identity = 2.0%

**From:** Lauren Ransome [lransome@aspb.org]  
**Sent:** Thursday, September 19, 2002 1:18 PM  
**To:** Guy.Birkenmeier@bakerbotts.com  
**Cc:** Melissa Junior; Nancy Winchester  
**Subject:** Date of Public Avail of PP Vol. 115 no.



Lauren A. Ransome  
Production Manager, *Plant Physiology*  
American Society of Plant Biologists  
15501 Monona Drive  
Rockville, MD 20855-2768 USA  
Phone: 301-251-0560 ext. 130  
Fax: 301-309-9196  
Email: [lransome@aspb.org](mailto:lransome@aspb.org)  
Web: [www.plantphysiol.org](http://www.plantphysiol.org)

<><><><><><><><><>

**Birkenmeier, Guy**

**From:** Birkenmeier, Guy  
**Sent:** Tuesday, September 17, 2002 8:21 AM  
**To:** 'nancyw@aspb.org'; 'mjunior@aspb.org'; 'lransome@aspb.org'  
**Subject:** Date of public availability of Plant Physiology vol.115 no.2

Dear Ms. Winchester, Ms. Junior, and Ms. Ransome:

What was the date on which the October 1997 issue of *Plant Physiology* (vol. 115, no. 2) became available to the public? Any information that you can provide will be helpful. Thank you.

Guy

Guy F. Birkenmeier, Ph.D.  
Scientific Advisor/Professional Support  
BAKER BOTTS L.L.P.  
30 Rockefeller Plaza  
New York, NY 10112  
T: 212.408.2572  
F: 212.408.2501

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AF002706	2522361	1	Nov 4 1997 0:12	Live
AF002706	2522361	1	Oct 15 1997 0:12	Dead

Accession AF002706 was first seen at NCBI on Oct 15 1997 0:12

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**Accession AF009657 was first seen at NCBI on Oct 15 1997 0:22**

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